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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,953	09/28/2005	Nobuko Uchida	17810-518 NATL	1069
30623 7590 12/17/2007 MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C. ONE FINANCIAL CENTER BOSTON, MA 02111			EXAMINER MACFARLANE, STACEY NEE	
			ART UNIT	PAPER NUMBER
			1649	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/524,953

Applicant(s)

UCHIDA ET AL.

Examiner

Stacey MacFarlane

Art Unit

1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 1-29, 35 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-34 and 37-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

***Election/Restrictions***

1. Applicant's election without traverse of Group III, claims 30-34 and 37-43 and the species of a combination of LIF and bFGF for claim 41, in the reply filed on October 25, 2007 is acknowledged.
2. Claims 1-29 and 35-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 25, 2007.
3. Claims 30-34 and 37-43, in so far as they read upon the elected species, will be examined upon their merits in the instant Office Action.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:  

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claims 30-34, 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. The term "further subdivided" in claim 30 is a relative term which renders the claim indefinite. The term "further" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of subdivision prior to performing the method. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

7. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the means by which "selecting" is performed. It is unclear if this step encompasses physically separating the cells, or if it reads upon the mental step of selecting based upon immunoreactivity. Absent a clarification, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, and it potentially raises issues of enablement as to "how" a skilled artisan would practice the claimed method.

8. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The claim recites a method of producing a subdivision of cells "which can initiate neurospheres", comprising contacting neural cells with an antibody that binds CD15 and selecting CD15<sup>+/lo</sup> cells. The omitted structural cooperative relationships are the structural characteristics and/or distinguishing features of cells "which can initiate neurospheres". Absent a clarification, one skilled in the art would not know how to distinguish the cells which "can" initiate from those that cannot.

9. Claims 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the means by which "further selecting" is performed (see also section 7 above).

10. Claims 34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active steps by which the method comprising "removing" the cells that "do not bind MMA" or cells that "are CD24<sup>+</sup>" are to be performed.

11. Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the means by which "further enriching" is performed.

12. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the means by which "selecting" is performed (see section 7 above) and the means by which "are enriched" is performed.

13. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active steps by which the method comprising "removing" the cells that are SC20<sup>+</sup> is to be performed.

14. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the means by which "selecting" is performed, the means by which "removing" is performed, and the steps required for "proliferating" cells.

15. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the means by which "selecting" is performed.

16. Claims 31 and 43 are indefinite for depending from indefinite claims.

***Claim Rejections - 35 USC § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 30, 31, 34 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Gocht et al. Anatomy and Embryology 186: 543-556, December 1992.

18. Claim 30 is drawn to a method of producing a population of cells enriched for human central nervous system stem cell (CNS-SC), progenitors or a combination thereof comprising contacting neural or neural derived cells with a monoclonal antibody that binds CD15 and selecting cells that are CD15<sup>-lo</sup>. Dependent claims recite wherein the cells are obtained from primary neural tissue (claim 31) and wherein the antibody recognizing CD15 is MMA (claim 34). Claim 39 recites a method comprising selecting cells that bind monoclonal MMA antibody.

19. The Gocht prior art teaches that the cluster determinant 15, consisting of a carbohydrate determinant specifically recognized by several monoclonal antibodies

(e.g. My-1, SSEA-1, VEP8, VEP9, VIM-C6 and MMA) was well known within the art as capable of identifying subpopulations of neural progenitor cells within the embryonic and adult CNS. The prior art specifically teaches contacting fetal (and adult – see lines 1-6 page 544) human primary brain tissue with MMA antibody and identifying subpopulations of neural progenitors that are “low” for CD15 immunoreactivity (Table 1). Absent evidence to the contrary, the prior art teaches the method of the claims comprising contacting and/or identifying or selecting neural or neural derived cells that are CD15<sup>-lo</sup>, wherein the cells are from primary neural tissue and the antibody is specifically MMA. Furthermore, the Gocht reference concludes that CD15 contributes to the complex interactions involved in cell adhesion and morphogenesis as further evidenced by the fact that disruption of CD15 leads to dedifferentiation and decompaction of embryonic cells (page 554, last two paragraphs).

### ***Claim Rejections - 35 USC § 103***

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. Claims 32, 33 and 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gocht et al. as applied to claims 30, 31, 34 and 39 above, and further in view of Uchida et al. PNAS 97(26): 14720-14725, published December 19, 2000 (citation C56 on IDS filed 10/30/2006).

23. Gocht et al teaches a method comprising contacting and/or selecting neural or neural derived cells that bind a monoclonal antibody that binds CD15, wherein the cells are from primary neural tissue and the antibody is specifically MMA.

24. Gocht does not teach the method further comprising contacting cells with a second monoclonal antibody SC20 (claims 32 and 41) or further comprising contacting cells with an anti-CD133 monoclonal antibody (claim 33) nor further comprising introducing the cells to a serum-free culture medium containing the instantly-elected LIF and bFGF (claim 41), however the Uchida et al. reference teaches methods comprising selecting cells that are SC20<sup>-lo</sup> (a.k.a. 8G1) and CD133<sup>+</sup> in order to "further enrich neurosphere initiating cell activity within the CD133<sup>+</sup> CD24<sup>-lo</sup> fraction" (second paragraph, page 14720). The Uchida prior art further teaches introducing Neurosphere-Initiating cells to serum-free media supplemented with both LIF and bFGF (paragraph 1, page 14722).

25. It would be obvious to one of ordinary skill in the art to combine the methods of identifying CD15<sup>-lo</sup> subpopulations of cells from primary tissue, as taught by Gocht et



al., with further subdivision and culture methods as taught by Uchida et al. One would be motivated to combine because the Gocht prior art identifies selective subpopulations of cells during human CNS development based upon their CD15 immunoreactivity and identifies CD15-negative cells as relatively undifferentiated as compared to CD15-positive cells. The Uchida reference teaches methods of isolating and enriching cultures of undifferentiated neural stem cells. Taken together, the method as taught by Gocht provides a means of identifying the cells that are the obvious starting material for the enrichment methods as taught by Uchida. Since each of the elements in combination are merely performing the same function as they did separately, then one of ordinary skill in the art would have been able to predictably combine the elements with a reasonable expectation of success (*KSR International Co. v. Teleflex, Inc.* 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007). Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

### ***Conclusion***

26. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M,W and ALT. F 6 am to 3 pm, T & R 5:30 am - 4 pm..

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane  
Examiner  
Art Unit 1649

/SNM/

  
OLGA N. CHERNYSHEV, PH.D.  
PRIMARY EXAMINER